REMARKS / ARGUMENTS

Claim Rejections 35 USC 112

Claims 10, 14, 22, 23, 26, 29 and 49 were rejected under 35 USC 112 as being indefinite.

Claims 10 and 14 have been amended so as to delete the references to the trade names and to incorporate the composition of "New Skin" as set out in the application as filed.

Claims 22 and 23 have been amended so as to replace the recitation "the polymer formulation" with the recitation "the liquid" for which clear antecedent basis is found in Claim 1.

Claims 26 and 49 have been amended so as to delete the phrase "such as a wound". This feature is the subject of new dependent Claims 52 and 53.

Claim 29 has been revised so as to recite more clearly the manner in which the mammalian cells are applied to the fibre scaffold.

Claim Rejections 35 USC 103

Claims 1-18, 20-28, 35, 36 and 49-51 were rejected under 35 USC 103 (a) as being unpatentable over *Coffee et al* (WO 98/03267) in view of *Shastri et al* (WO 97/16545).

Claim 1

Claim 1 as amended requires:

> A method of enabling growth of mammalian cells, which method comprises: supplying liquid comprising biologically compatible polymer to a liquid outlet in the vicinity of a surface and subjecting liquid issuing from the outlet to an electric field to cause the liquid to form polymer fibre which is attracted to and deposits onto the surface to form a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a given fibre diameter with gaps between adjacent fibre portions; and applying mammalian cells to the fibre scaffold, wherein the gaps between the fibre portions and the fibre diameter have a size relative to a diameter of the mammalian cells so as to facilitate at least one cell process selected from the group consisting of growth preferentially along the fibre portions, attachment to the fibre portions, elongation preferentially along the fibre portions, and differentiation.

The subject matter of Claim 1 is in no way disclosed or suggested by the documents cited by the Examiner.

Coffee et al describes a dispensing device and method for forming at least partially solid or gel-like material from a liquid. In one example, at least one liquid issuing from an outlet is subjected to an electric field causing the liquid to form at least one electrically charged jet which after formation, forms a fibre or breaks up into fibre fragments. The thus–formed at least partially solid or gel like material may be deposited, by virtue of the energy in the electric field, directly onto a surface area, for example an area skin enabling the formation of a dressing for a wound or a burn.

Nothing in *Coffee et al* discloses or suggests the formation of a polymer fibre scaffold comprising a three dimensional continuous network of intercommunicating fibre portions having a given fibre diameter with gaps between the adjacent fibre portions wherein the gaps between the fibre portions and the fibre diameter have a size relative to a diameter of the mammalian cells so as to facilitate at least one cell process

selected from the group consisting of growth preferentially along the fibre portions, attachment to the fibre portions, elongation preferentially along the fibre portions, and differentiation.

The Examiner has referred to various passages of *Coffee et al* as giving examples of fibre diameter. These examples are, however, given in the context of enabling provision of a would dressing that (see the paragraph bridging pages 17 and 18 on the subsequent paragraph) provides good coverage to protect the wound while allowing air to pass through the dressing and puss and other detritus to pass from the wound, while preventing ingress of bacterial matter into the wound. There is no disclosure in *Coffee et al* that the gaps between the fibre portions and the fibre diameter should have a size relative to a diameter of the mammalian cells so as to facilitate at least one cell process as set out in Claim 1. Indeed there is no teaching in *Coffee et al* that the fibre diameter let alone the gap between the fibre portions may be important for facilitating at least one cell process. Further, although *Coffee et al* gives various examples of fibre diameters, all of these examples are completely silent as to the size of the gap between the fibre portions. There is thus no teaching whatsoever in *Coffee et al* of providing a fibre scaffold wherein the gaps between the fibre portions and the fibre diameter have a size relative to a diameter of mammalian cells so as to facilitate at least one cell process as set out in claim 1.

Shastri et al (WO97/16545) is concerned with the use of electrically conducting biocompatible polymers to achieve electrical stimulation of nerve cells. Numerous methods for synthesising the polymer are described which result in the production of polymer films, layers or multi-layers (page 10 line 22 to page 11 line 19, page 11 line 31 to page 39 line 27, for example). As another possibility, the electrically conducting polymer of *Shastri et al* may be blended with another polymer material and applied as a coating. In a further example, *Shastri et al* suggests that a textile fibre may be coated with an electrically conducting polymer film of polypyrrole and polyaniline (page 11 lines 20-30). Although the text at page 40 lines 31 and 32 suggests that a scaffold may be formed, the text at page 50 lines 29-32 clearly teaches that the scaffold should be made

of material other than the electrically conducting polymer. *Shastri et al* also teaches that, for in vitro culture, the electrically conducting polymer can be used as a coating on or can be blended with polymers forming culture flask, wells, beads or other cartridge containers, for example formed of plastic such as polystyrene, polypropylene and polyterepthalate (see page 16 lines 7-10).

By describing many different physical forms including thin films, laminates and coatings for the electrically conducting polymer, *Shastri et al* teaches that the physical form of the polymer is not important; rather what is important in *Shastri et al* is that the polymer should be electrically conductive to enable electrical stimulation of nervous cells.

There is no disclosure in *Shastri et al* of subjecting liquid issuing from an outlet to an electric field to cause the liquid to form polymer fibre which is attracted to and deposits onto a surface to form a polymer fibre scaffold comprising a three dimensional continuous network of intercommunicating fibre portions let alone of forming such a polymer fibre scaffold such that the gaps between the fibre portions and the fibre diameter have a size in relation to a diameter of mammalian cells that facilitates at least one cell process as set out in Claim 1. Rather, as set out above, *Shastri et al* is specifically concerned with the use of electrically conducting polymer to enable electrical stimulation of nerve cells.

Absent the hindsight available to the Examiner from having read the present application, the person skilled in the art would never consider combining the disclosures of *Shastri et al* and *Coffee et al* because Coffee et al is primarily concerned with wound care while *Shastri et al* is concerned with electrical stimulation of nerve cells. Furthermore, even if a person skilled in the art were directed to try and combine the disclosures of *Shastri et al* and *Coffee et al* he would not be able to arrive at the inventive concept claimed in amended Claim 1 because, for example, neither *Shastri et al* nor *Coffee et al* teaches subjecting liquid issuing from an outlet to an electric field to cause the liquid to form polymer fibre which is attracted to and deposits onto a surface

to form a polymer fibre scaffold comprising a three dimensional continuous network of intercommunicating fibre portions such that the gaps between the fibre portions and the fibre diameter both have a size relative to a diameter of mammalian cells that facilitates at least one cell process as set out in Claim 1.

Claims 2-13

Claims 2-13 are dependent on Claim 1 and should be allowable for the same reasons as Claim 1.

Claim 14

Claim 14 requires formation in the manner set out in claim 14 of a polymer fibre scaffold comprising a three dimensional continuous network of intercommunicating fibre portions having a fibre diameter in the range of 1-2 microns with gaps between adjacent fibre portions wherein the gaps between the fibre portions and the fibre diameter are such that human fibroblast cells grow or elongate preferentially along the fibre of these scaffolds.

For the reasons set out in above in relation to Claim1, nothing in *Coffee et al* and *Shastri et al* would lead a person skilled in the art to the subject matter claimed in Claim 14. For example, nothing in *Coffee et al* and *Shastri et al* would lead a person skilled in the art to production of a polymer fibre scaffold when the gaps between the fibre portions and the fibre diameter are such that human fibroblast cells grow or elongated preferentially along the fibre diameter of the scaffold. Indeed, as set out above, nothing in either *Coffee et al* or *Shastri et al* attaches any importance to the fibre diameter and the fibre gap size.

Claim 16

Claim 16 requires, amongst other features, formation of a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a fibre of diameter and a gap between fibre portions that, without addition of extrinsic biological factors, facilitate differentiation. For the reasons explained above in

relation to claim 1, neither *Coffee et al* nor *Shastri et al* attaches any importance to the fibre diameter and the fibre gap size let alone suggests that the fibre diameter and fibre gap size may, without addition of extrinsic biological factors, facilitate differentiation.

Claim 17

Claim 17 is dependent on Claim 16 and should be allowable for the same reasons as Claim 16.

Claim 18

Neither *Coffee et al* nor *Shastri et al* is concerned with facilitating differentiation of osteogenic stem cells to produce cells having a morphology resembling nerve cells and nothing in *Coffee et al* or *Shastri et al* teaches or even hints that this could be achieved by applying the osteogenic stem cells without addition of extrinsic biological factors to a polymer fibre scaffold formed in the manner set out in claim 18 so that the polymer scaffold comprises a three dimensional continuous network of intercommunicating fibre portions having a fibre diameter of about 10 microns with gaps between adjacent fibre portions of about 16 microns. Indeed nothing whatsoever in *Coffee et al* or *Shastri et al* suggests this particular combination of fibre diameter and gap size.

Claim 19

Claim 19 is dependent on Claim 16 and should be allowable for the same reasons as Claim 16.

Claim 20

Claim 20 requires formation in the manner set out in claim 20 of a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a fibre diameter in the range from 0.2 to 100 microns and a gap size between adjacent fibre portions in the range from about 10 to 500 microns; and applying mammalian cells to the fibre scaffold, the fibre diameter and gap size being such as to

facilitate at least one cell process selected from the group consisting of growth preferentially along the fibre portions, attachment to the fibre portions, elongation preferentially along the fibre portions, and differentiation.

For the reasons set out above in relation to claim 1, nothing in either *Coffee et al* nor *Shastri et al* even hints at the subject matter of claim 20.

Claim 21

Claim 21 requires formation in the manner set out in claim 21 of a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a fibre diameter in the range from 2 to 500 microns and a gap size between adjacent fibre portions in the range from about 25 to 3000 microns; and applying mammalian cells to the fibre scaffold, the fibre diameter and gap size being such as to facilitate at least one cell process selected from the group consisting of growth preferentially along the fibre portions, attachment to the fibre portions, elongation preferentially along the fibre portions, and differentiation.

For the reasons set out above in relation to claim 1, nothing in *Coffee et al* or *Shastri et al* even hints at the subject matter of claim 21.

Claim 15

Claim 15 is dependent on Claim 20 and should be allowable for the same reasons as Claim 20 while Claims 22 and 23 are dependent on Claim 1 and should be allowed for the same reasons as Claim 1.

Claim 24

Claim 24 requires formation in the manner set out in claim 24 of a polymer fibre-scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a fibre diameter in the range of from 20 to 70 microns and a gap size between adjacent fibre portions in the range of 100 to 500 microns. Nothing in *Coffee et al* or *Shastri et al* even hints at the subject matter of claim 24.

Claims 25, 26, 27 to 30, 35 and 36

Claims 25 and 26 are dependent on Claim 24 and should be allowable for the same reasons as Claim 24 while Claims 27-30 are dependent on Claim 1 and should be allowable for the same reasons as Claim 1. Similarly, Claims 35 and 36 are dependent on Claim 1 and should be allowable for the same reasons as Claim 1.

Claims 1 to 30, 35, 36 and 49 to 51

Claims 1 to 30, 35, 36 and 49 to 51 were rejected under 35 USC 103(a) as being unpatentable over *Coffee et al* and *Shastri et al* in view of *Smith et al* (WO 01/27365) and *Simpson et al* (WO02/40242).

For the reasons set out above, *Coffee et al* and *Shastri et al* in no way suggest or even hint at the subject matter of Claims 1 to 30, 35, 36 and 49 to 51 and for the reasons set out below *Smith et al* does not provide the features missing from *Coffee et al* and *Shastri et al*.

Smith et al describes an article of manufacture such as a wound dressing comprising electro-spun fibres spun from a substantially homogenous mixture containing at least one hydrophillic polymer, at least one polymer that is at least weakly hydrophobic and optionally at least one pH adjusting compound. The aim of *Smith et al* is to avoid a local pH change to an undesirable pH environment that may cause side effects such as slow wound healing. *Smith et al* gives various examples of fibre diameter and pore size. These examples are, however, given in the context of providing a wound dressing that enables a wound to be kept clean by preventing bacterial infection penetration by aerosol particle capture mechanisms and possibly hindering passage of viral particles (page 12 lines 18-28 and page 13 lines 14-22). There is no suggestion of formation of a polymer fibre scaffold comprising a three dimensional continuous network of intercommunicating fibre portions wherein the fibre diameter and the gaps between the fibre portions have a size relative to a diameter of mammalian cells so as to facilitate at least one cell process as set out in claim 1.

Indeed there is no mention in *Smith et al* in any context of cells. Rather, Smith et al is simply concerned with a wound dressing.

Shastri et al is, as set out above, specifically concerned with the use of electrically conducting polymer to enable electrical stimulation of nerve cells while *Coffee et al* and *Smith et al* are concerned with the formation of wound dressings. Absent with hindsight available to the Examiner from having read the present application, a person of skill in the art would never consider combining these three documents. Even a person skilled in the art directed to try and combine the disclosures of these documents would not, for the reasons as set out above, arrive at the subject matter of the claimed invention.

For the reasons set out above, the features missing from *Smith et al* are not shown by *Coffee et al* or *Shastri et al* and accordingly the subject matter of Claim 1 is patentable over the combination of *Coffee et al*, *Shastri et al* and *Smith et al*.

As regards claims 2 to 30, 35, 36 and 49 to 51, for the reasons set out above, the features missing from *Smith et al* are not shown by *Coffee et al* or *Shastri et al* and accordingly the subject matter of Claim 1 is patentable over the combination of *Coffee et al*, *Shastri et al* and *Smith et al*.

As regards the examiner's specific comments, *Smith et al* simply teaches that polycaprolactone may be used for formation of a wound dressing. For the reasons set out above, *Smith et al* does not provide the features of claims 1, 14 and 16 missing from *Coffee et al* and *Shastri et al*. Claims 10 and 19 are dependent on claims 1 and 16, respectively, and therefore are patentable over the combination of *Coffee et al*, *Shastri et al* and *Smith et al*.

For the reasons set out above, *Coffee et al* and *Shastri et al* in no way suggest or even hint at the subject matter of Claims 1 to 30, 35, 36 and 49 to 51 and for the

reasons set out below *Simpson et al* does not provide the features missing from *Coffee et al* and *Shastri et al.*

Simpson et al is a very lengthy document concerned specifically with the electro-processing of collagen. This document adds nothing else to the teaching of *Coffee et al* and *Shastri et al.* Nothing in *Simpson et al* teaches or even hints at the formation in the manner set out in claim 1 of a polymer fibre which is attracted to and deposits onto the surface to form a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a given fibre diameter with gaps between adjacent fibre portions; and applying mammalian cells to the fibre scaffold, wherein the gaps between the fibre portions and the fibre diameter have a size relative to a diameter of the mammalian cells so as to facilitate at least one cell process selected from the group consisting of growth preferentially along the fibre portions, attachment to the fibre portions, elongation preferentially along the fibre portions, and differentiation. *Simpson et al* suggests that cells will migrate through pores in collagen structures of a size as small as 3.7microns. However, there is nothing in *Simpson et al* that would teach a person skilled in the art to form a polymer fibre scaffold in the manner set out in claim 1 so that the gaps between the fibre portions and the fibre diameter have a size relative to a diameter of the mammalian cells so as to facilitate at least one cell process selected from the group consisting of growth preferentially along the fibre portions, attachment to the fibre portions, elongation preferentially along the fibre portions, and differentiation.

As regards the examiner's specific comments concerning claims 29 and 30, these claims are dependent on claim 1 and should be allowable for the same reasons as claim 1.

CONCLUSION

For the reasons set forth above, it is respectfully submitted that all claims remaining in the application are now in condition for allowance.

In the event the Examiner considers personal contact advantageous to the disposition of this case, the Examiner is requested to contact the undersigned at (614) 424-4293.

Respectfully submitted,

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